

=> file wpids

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>>>UPDATE WEEKS:

MOST RECENT DERWENT WEEK 9624 <199624/DW>

DERWENT WEEK FOR CHEMICAL CODING: 9612

DERWENT WEEK FOR POLYMER INDEXING: 9620

DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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=> s fox, g?/au or fox g?/au

30 FOX, G?/AU

30 FOX G?/AU

L1 30 FOX, G?/AU OR FOX G?/AU

=> s ciossek, t?/au or ciossek t?/au

0 CIOSEK, T?/AU

0 CIOSEK T?/AU

L2 0 CIOSEK, T?/AU OR CIOSEK T?/AU

=> s ullrich, a?/au or ullrich a?/au

33 ULLRICH, A?/AU

33 ULLRICH A?/AU

L3 33 ULLRICH, A?/AU OR ULLRICH A?/AU

=> s millauer, b?/au or millauer b?/au

1 MILLAUER, B?/AU

1 MILLAUER B?/AU

L4 1 MILLAUER, B?/AU OR MILLAUER B?/AU

=> s kinase?

L5 1484 KINASE?

=> s l1 and l5

L6 1 L1 AND L5

=> s l5 and (l3 or l4)

L7 12 L5 AND (L3 OR L4)

=> d l6 bib,abs 1

L6 ANSWER 1 OF 1 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD

AN 95-373799 [48] WPIDS

DNN N95-275604 DNC C95-161991

TI New nucleic acid encoding EPH-like receptor tyrosine kinase  
(s) - and related vectors, host cells, proteins, antibodies etc.,  
used diagnostically and therapeutically to modulate receptor  
activation or prodn..

DC B04 D16 S03

IN FOX, G M; JING, S; WELCHER, A A

PA (AMGE-N) AMGEN INC

\*< Arti Shah- Stic Searcher- 308-4259 >\*

CYC 62

PI WO 9528484 A1 951026 (9548)\* EN 135 pp  
 RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE  
 SZ UG  
 W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP  
 KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO  
 RU SD SE SG SI SK TJ TM TT UA UG UZ VN

AU 9522925 A 951110 (9607)

ADT WO 9528484 A1 WO 95-US4681 950414; AU 9522925 A AU 95-22925 950414

FDT AU 9522925 A Based on WO 9528484

PRAI US 94-229509 940415

AN 95-373799 [48] WPIDS

AB WO 9528484 A UPAB: 960108

An isolated nucleic acid (I) encoding a polypeptide (II) with at least one of the biological activities of an EPH-like receptor protein tyrosine kinase (RPTK), is claimed. It has one of 2962, 2162, 3116 or 4529 bp nucleic acid sequences given in the specification (it may also be a complementary strand, hybrid, or degenerate hybrid of these).

USE - Transformed cells are used to express EPH-like RPTK for therapeutic or diagnostic use, including targeted expression in selected tissue. (IIa), esp. in soluble form, can be used to modify endogenous activation of RPTK, while synthesis of these receptors can be modulated by oligonucleotides antisense to (I), e.g. to alter proliferation and/or differentiation of receptor bearing cells. Abs can be used diagnostically to modulate receptor activation, and to isolate cells bearing EPH-like receptors (these are potentially useful in the treatment of patients deficient in specific cell types). (I) or its fragments can be used in hybridisation assays, or to detect genetic abnormalities.

Dwg.0/11

=&gt; d 17 bib,abs 1-12

L7 ANSWER 1 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD

AN 96-077343 [08] WPIDS

DNN N96-064355 DNC C96-025580

TI Treating tyrosine kinase signal transduction associated cellular proliferation disorders - by introducing DNA encoding signalling incompetent inositol 1, 4, 5-tri phosphate receptor, which competes with endogenous receptor.

DC B04 D16 S03

IN FISCHER, G A; ULLRICH, A

PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN

CYC 63

PI WO 9600586 A2 960111 (9608)\* EN 126 pp

RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE  
 SZ UG

W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS  
 JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT  
 RO RU SD SE SG SI SK TJ TM TT UA UZ VN

AU 9529789 A 960125 (9617)

WO 9600586 A3 960215 (9622)

ADT WO 9600586 A2 WO 95-EP2532 950629; AU 9529789 A AU 95-29789 950629;

WO 9600586 A3 WO 95-EP2532 950629

\*&lt; Arti Shah- Stic Searcher- 308-4259 &gt;\*

FDT AU 9529789 A Based on WO 9600586

PRAI US 94-268390 940630

AN 96-077343 [08] WPIDS

AB WO 9600586 A UPAB: 960227

Inhibiting the effects of inositol 1, 4, 5-triphosphate (IP3) receptor-mediated signal transduction by an endogenous IP3 protein in a cell comprises, delivering a DNA molecule encoding a signalling-incompetent (SI) form of the IP3 receptor protein to the cell, so that the SI form is produced and competes with the endogenous receptor for access to molecules in the IP3 receptor protein signalling pathway, which activate, or are activated by the endogenous IP3 receptor protein.

USE - The method of (1) can be used to treat conditions associated with abnormalities in tyrosine kinase signal transduction, by administering a cpd. that inhibits IP-3 receptor activity (claimed). The methods of (2) and (3) can be used to detect cpds. capable of modulating IP3 receptor signal transduction, and molecules capable of binding the IP3 receptor, such cpds. molecules and the method of (1) can be used to inhibit inappropriate cell growth associated with tyrosine kinase receptor signal transduction abnormalities, including cancer, psoriasis (claimed) and atherosclerosis.

ADVANTAGE - The introduction of SI IP3 receptor mutants to normal cells does not have a negative effect on cell growth or survival, and the suppression of transforming activities is not oncogene specific.

Dwg.0/8

L7 ANSWER 2 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD

AN 95-382959 [49] WPIDS

DNC C95-165522

TI New poly nucleotide(s) encoding megakaryocyte tyrosine kinase(s) - used to develop prods. for the treatment and diagnosis of kinase related signal transduction abnormalities..

DC B04 D16

IN GISHIZKY, M; SURES, I; ULLRICH, A

PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN; (SUGE-N) SUGEN INC

CYC 61

PI WO 9529185 A1 951102 (9549)\* EN 82 pp

RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG

W: AM AU BB BG BR BY CA CN CZ EE FI GE HU IS JP KE KG KR KZ LK LR LT LV MD MG MN MW MX NO NZ PL RO RU SD SG SI SK TJ TT UA UZ VN

AU 9523625 A 951116 (9608)

ADT WO 9529185 A1 WO 95-US5008 950424; AU 9523625 A AU 95-23625 950424

FDT AU 9523625 A Based on WO 9529185

PRAI US 95-426509 950421; US 94-232545 940422

AN 95-382959 [49] WPIDS

AB WO 9529185 A UPAB: 951211

Isolated polynucleotide (PN) (I) encoding a megakaryocyte kinase-1 (MKK1) protein, is claimed. Also claimed are: (1) isolated PNs encoding MKK2 and 3 proteins; (2) a recombinant DNA vector contg. a PN sequence that encodes a MKK1, 2 or 3 protein; (3)

\*< Arti Shah- Stic Searcher- 308-4259 >\*

an engineered host cell that contains a recombinant DNA vector as in (2); (4) an antisense molecule contg. a sequence complementary to at least a part of the coding sequence of a MKK1, 2 or 3 protein, which inhibits translation of the MKK1, 2 or 3 mRNA in a cell; (5) an isolated recombinant MKK1, 2 or 3; (6) a fusion protein comprising MKK1, 2 or 3 linked to a heterologous protein or peptide sequence; and (7) a monoclonal antibody (MAB) which binds to an epitope of MKK1, 2 or 3.

USE - The prods. and methods can be used in the treatment and diagnosis of diseases resulting from abnormalities in MKK signal transduction pathways. They can also be used to treat leukaemia and thrombocytopenia, or for the ex vivo culture of megakaryocytes for the autologous treatment of patients receiving chemotherapy, or other therapies which deplete megakaryocytes and platelets.  
Dwg.0/14

L7 ANSWER 3 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD  
AN 95-366151 [47] WPIDS  
DNN N95-270939 DNC C95-159332  
TI Treatment of a disease or condition characterised by abnormality in a signal transduction pathway - by disrupting or promoting the interaction in vivo.  
DC B04 S03  
IN HOBERT, O; JALLAL, B; KOSTKA, G; OBERMEIER, A; ULLRICH, A  
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN  
CYC 63  
PI WO 9526983 A2 951012 (9547)\* EN 100 pp  
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG  
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NL NO NZ PL PT RO RU SD SE SG SI SK TJ TT UA US UZ VN  
AU 9522334 A 951023 (9605)  
WO 9526983 A3 960208 (9622)  
ADT WO 9526983 A2 WO 95-US3945 950330; AU 9522334 A AU 95-22334 950330;  
WO 9526983 A3 WO 95-US3945 950330  
FDT AU 9522334 A Based on WO 9526983  
PRAI US 94-291591 940815; US 94-221642 940331; US 94-251691 940531  
AN 95-366151 [47] WPIDS  
AB WO 9526983 A UPAB: 951128  
Treatment of a disease or condition is claimed, where the disease or condition is characterised by an abnormality in a signal transduction pathway involving the interaction between: (a) a receptor tyrosine kinase of the Trk family and a signalling component; (b) a heterogeneous ribonucleoprotein MP domain and a SH3 domain; (c) a MP domain and a vav protein SH3 domain; or (d) a SH3 domain and a DYN domain by disrupting or promoting the interaction in vivo.  
USE - The method is useful for screening, diagnosing and treating diseases, such as neurodegenerative or neuroproliferative disorders or cancer (claimed). Screening methods for agents useful to treat such diseases are also provided.  
Dwg.0/3

L7 ANSWER 4 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD

\*< Arti Shah- Stic Searcher- 308-4259 >\*

AN 95-320318 [41] WPIDS  
DNN N95-240968 DNC C95-142264  
TI Modulating signal transduction of insulin receptor type tyrosine kinase - by inhibiting its de-phosphorylation by reactor protein phospho-tyrosine phosphatase, also methods for identifying inhibitors useful for treating diabetes mellitus.  
DC B04 D16 S03  
IN KHARITONENKOV, A E; LAMMERS, R; SAP, J M; SCHLESSINGER, J; ULLRICH, A  
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN; (UYNV) UNIV NEW YORK STATE  
CYC 60  
PI WO 9523217 A2 950831 (9541)\* EN 74 pp  
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG  
W: AM AU BB BG BR BY CA CN CZ EE FI GE HU JP KE KG KR KZ LK LR LT LV MD MG MN MW MX NO NZ PL RO RU SD SG SI SK TJ TT UA UZ VN  
AU 9519765 A 950911 (9550)  
ADT WO 9523217 A2 WO 95-US2619 950228; AU 9519765 A AU 95-19765 950228  
FDT AU 9519765 A Based on WO 9523217  
PRAI US 94-203189 940228  
AN 95-320318 [41] WPIDS  
AB WO 9523217 A UPAB: 951019  
Modulating signal transduction mediated by an insulin receptor type tyrosine kinase (A) comprises inhibiting dephosphorylation of (A) by a receptor protein phosphotyrosine phosphatase (B). Also claimed are: (1) a method for detecting or quantifying complex (C) formed between receptor-type protein tyrosine phosphatase (RPTP) alpha or epsilon and (A); (2) a method for identifying or isolating cpds. able to bind to (C); (3) a method for identifying cpds. that block formation of (C); (4) a method for identifying cpds. that modulate (A)-mediated signal transduction by modulating activity of RPTP alpha or epsilon; (5) compsns. for treating or preventing diabetes mellitus types I and II contg. antisense RPTP alpha or epsilon nucleic acid molecules and a carrier.  
USE - Modulation can be used to stimulate or mimic signal transduction. Cpds. identified by method (4) can be used to treat diabetes or (not claimed) other diseases caused by dysfunctional signal transduction by (A). Also contemplated (not claimed) is gene therapy to generate deletion or missense RPTP mutants that interact with (A) but do not function in signal transduction. No dosage is given. Therapeutic cpds. can be administered by injection or orally.  
ADVANTAGE - The identified modulators should be of low toxicity since they are specific for (B) associated with the insulin receptor but do not affect other (B). Dephosphorylation of (A) is inhibited even in absence of insulin.  
Dwg.0/8

L7 ANSWER 5 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD  
AN 95-311540 [40] WPIDS  
DNC C95-138756  
TI Cell lines useful for the screening and identification of cpds. - through modulation of phospho-tyrosine phosphatase activity and insulin receptor tyrosine kinase mediated signal

transduction.

DC B04 D16  
 IN HOPPE, E; MOLLER, N P H; ULLRICH, A  
 PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN  
 CYC 61  
 PI WO 9523231 A1 950831 (9540)\* EN 38 pp  
 RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE  
 SZ UG  
 W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP  
 KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NL NO NZ PL PT  
 RO RU SD SE SG SI SK TJ TT UA UZ VN

AU 9518125 A 950911 (9550)  
 ADT WO 9523231 A1 WO 95-EP731 950228; AU 9518125 A AU 95-18125 950228  
 FDT AU 9518125 A Based on WO 9523231  
 PRAI US 94-203218 940228  
 AN 95-311540 [40] WPIDS  
 AB WO 9523231 A UPAB: 951011

A genetically engineered mammalian cell (I) contains:(a) a first nucleic acid mol. having a nucleotide sequence which encodes a protein phosphotyrosine phosphatase (PTP) or its fragment, operatively associated with an element that controls its expression, and(b) a second nucleic acid mol. which encodes an insulin receptor protein tyrosine kinase (IR-PTK), or its fragment, operatively associated with an element that controls its expression, where a PTP and an IR-PTK are co-expressed by the mammalian cell.

Also claimed are: (1) a method for determining whether a cpd. is capable of modulating IR-PTK signal transduction by modulating phosphotyrosine phosphatase activity of receptor protein tyrosine phosphatases alpha (RPTPs) or RPTP epsilon, comprises:(a) contacting the cpd. with a whole live or fixed (I), for an interval sufficient for the cpd. to modulate the signal transduction;(b) measuring the signal transduction, and(c) comparing the signal transduction to that incubated without the cpd.;(2) a method for identifying a nucleic acid mol. encoding a gene product which is capable of modulating IR-PTK signal transduction by modulating the enzymatic activity of phosphotyrosine phosphatase, comprising:(a) introducing the nucleic acid mol. into (I);(b) culturing the cells so that the gene product encoded by the nucleic acid mol. is expressed in the cells and interacts with the phosphotyrosine phosphatase and IR-PTK or its deriv.:(c) measuring the signal transduction, and(d) comparing the signal transduction to that in the cells without the nucleic acid mol., thereby determining whether the gene product encoded by the nucleic acid mol. is capable of modulating signal transduction;(3) a method for isolating from a mixt. the nucleic acid mol. described in (2), comprising steps (a) to (d) from (2), and(e) selecting and culturing the cells identified in (d) and recovering the nucleic acid mol., thereby isolating the nucleic acid mol..

USE - (I) are used to screen and identify non-toxic cpds. that could elicit or modulate insulin signal transduction even in the absence of insulin (claimed), therefore, (I) are useful in screening assays for non-toxic cpds. that, by modulating phosphatase activity, modulate or prolong IR-PTK signal transduction. The methods have uses in the treatment of diabetes.  
 Dwg.0/3

L7 ANSWER 6 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD  
AN 95-263705 [34] WPIDS  
DNC C95-120078  
TI Treatment of, e.g., cancers, atherosclerosis or fibrotic disorders -  
by admin. of an inhibitor of platelet derived growth factor  
receptor.  
DC B05  
IN BAJOR, T; GAZIL, A; HAIMICHAEL, J; HIRTH, K P; KABBINAVAR, F F;  
KERI, G; LAMMERS, R; LEVITZKI, A; MANN, E; ORFI, L; SCHWARTZ, D P;  
SHAWVER, L K; SLAMON, D J; SZEKELY, I; TANG, C P; ULLRICH, A; GAZIT,  
A  
PA (BIOS-N) BIOSIGNAL LTD; (PLAC) MAX PLANCK GES FOERDERUNG  
WISSENSCHAFTEN; (SUGE-N) SUGEN INC; (REGC) UNIV CALIFORNIA; (YISS)  
YISSUM RES & DEV CO  
CYC 59  
PI WO 9519169 A2 950720 (9534)\* EN 15 pp  
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE  
SZ  
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP  
KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NL NO NZ PL PT  
RO RU SD SE SI SK TJ TT UA UZ VN  
AU 9515633 A 950801 (9546)  
WO 9519169 A3 960215 (9622)  
ADT WO 9519169 A2 WO 95-US363 950106; AU 9515633 A AU 95-15633 950106;  
WO 9519169 A3 WO 95-US363 950106  
FDT AU 9515633 A Based on WO 9519169  
PRAI US 94-179570 940107  
AN 95-263705 [34] WPIDS  
AB WO 9519169 A UPAB: 950904  
Treatment of cell proliferative disorders characterised by  
inappropriate PDGF-R activity, comprising admin. of a compsn.  
comprising a cpd. of formula e.g. (I)-(III), or an active drug form  
or salt of these cpds., which significantly inhibits one or more  
PDGF-R activities in vitro or in vivo.  
In cpds. (I): R1, R2, R2', R2'', R2''' = H, halo, trihalomethyl  
or NO2; R3 = H, carboxy or carbalkoxy. In cpds. (II): R4, R5 = halo,  
H, trihalomethyl or NO2; R6 = aryl, alkyl, alkenyl or alkynyl. (c)  
in cpds. (III): R7, R7', R8 = halo, OH, H, alkoxy, SH, NH or CMe3;  
R9 = aryl or H.  
USE - The cpds. inhibit PDGF-R (platelet derived growth factor  
receptor) activity and the activity of PDGF-R related  
kinases Flt, Flk and KDR. They may be used to treat cancers  
(e.g. intra-axial brain cancer, ghoma, ovarian cancer, colon cancer,  
prostate cancer, lung cancer, Kasposi's sarcoma or melanoma), blood  
vessel proliferative disorders (e.g. atherosclerosis), or fibrotic  
disorders (e.g. hepatic fibrotic disorders or mesangial cell  
proliferative disorders).  
Admin. is, e.g., oral, parenteral, or topical. Dosage is  
0.02-25 (esp. 0.2-15) mg/kg/day.  
Dwg.0/5  
  
L7 ANSWER 7 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD  
AN 95-224055 [29] WPIDS  
CR 95-224054 [26]

DNN N95-175673 DNC C95-103045  
 TI New nucleic acid encoding CCK-2 receptor tyrosine kinase -  
 and derived vectors, transformed cells, proteins and antibodies,  
 useful for diagnosis and treatment of proliferative and nervous  
 system diseases and for screening modulators.  
 DC B04 D16 S03  
 IN ALVES, F H E; ULLRICH, A  
 PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN  
 CYC 58  
 PI WO 9514089 A2 950526 (9529)\* EN 115 pp  
 RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE  
 SZ  
 W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP  
 KE KG KP KR KZ LK LR LT LU LV MD MG MN MW NL NO NZ PL PT RO  
 RU SD SE SI SK TJ TT UA UZ VN  
 AU 9481439 A 950606 (9538)  
 ADT WO 9514089 A2 WO 94-EP3799 941116; AU 9481439 A AU 94-81439 941116  
 FDT AU 9481439 A Based on WO 9514089  
 PRAI US 93-153397 931116  
 AN 95-224055 [29] WPIDS  
 CR 95-224054 [26]  
 AB WO 9514089 A UPAB: 950727  
 Isolated nucleic acid (I) encoding a protein of the CCK-2 family  
 that contains an intracellular tyrosine kinase domain  
 (TKD) and an extracellular discoidin I domain (DID) is new. Also new  
 are (1) isolated, esp. cDNA, sequences encoding a CCK-2 protein,  
 including its alternatively spliced isoforms; (2) recombinant DNA  
 vector encoding a CCK-2 protein, or its fusion proteins; (3)  
 engineered host cells contg. these vectors; (4) isolated recombinant  
 CCK-2 receptor protein; (5) fusion protein of CCK2 linked to a  
 heterologous protein or peptide, (6) oligonucleotides that encode an  
 antisense sequence complementary to (I) able to inhibit translation  
 of the CCK-2 gene; (7) monoclonal antibodies (Ab) binding  
 specifically to an epitope or CCK-2; (8) methods for screening and  
 identifying (ant)agonists of CCK-2; (9) recombinant vector encoding  
 a truncated CCK-2 with dominant negative activity, able to inhibit  
 biological activity of CCK-2; (10) engineering cells contg. the  
 vector of (9), and (11) the truncated CCK-2 described in (9). The  
 specification includes a 3157bp cDNA sequence for CCK-2, and the  
 corresp. encoded 855 amino acid protein.  
 USE - Cells expressing CCK-2 are used to isolate cpds. that  
 inhibit or mimic activity of CCK-2 on cells; such cpds. are  
 potentially useful for treatment of proliferative diseases (e.g.  
 cancer) and nervous system diseases (e.g. Alzheimer's or Parkinson's  
 diseases, multiple sclerosis, muscular dystrophy, etc.). Ab and the  
 antisense sequences can also be used to modulate (esp. reduce)  
 endogenous activity of the CCK-2 receptor, and Ab may also be  
 attached to a cytotoxin or radioisotope for therapeutic use or for  
 in vivo imaging of tumours and metastases. (I) can be used  
 diagnostically to detect aberrant gene expression (e.g. in  
 hybridisation tests on biopsy samples). The truncated CCK-2 partic.  
 expressed from a retroviral vector, can also be used to modulate  
 CCK-2 activity.  
 Dwg.0/7



L7 ANSWER 8 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD  
 AN 95-224054 [29] WPIDS  
 CR 95-224055 [26]  
 DNN N95-175672 DNC C95-103044  
 TI New nucleic acid encoding MCK-10 receptor tyrosine kinase  
 - and derived vectors, transformed cells, proteins and antibodies  
 useful for diagnosis and treatment of proliferative disease, esp.  
 cancer, and for screening modulators.  
 DC B04 D16 S03  
 IN ALVES, F H E; ULLRICH, A  
 PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN  
 CYC 58  
 PI WO 9514088 A1 950526 (9529)\* EN 94 pp  
 RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE  
 SZ  
 W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP  
 KE KG KP KR KZ LK LR LT LU LV MD MG MN MW NL NO NZ PL PT RO  
 RU SD SE SI SK TJ TT UA UZ VN  
 AU 9481438 A 950606 (9538)  
 ADT WO 9514088 A1 WO 94-EP3797 941116; AU 9481438 A AU 94-81438 941116  
 FDT AU 9481438 A Based on WO 9514088  
 PRAI US 93-153397 931116  
 AN 95-224054 [29] WPIDS  
 CR 95-224055 [26]  
 AB WO 9514088 A UPAB: 950727  
 Isolated nucleic acid (I) encoding an MCK-10 (mammary carcinoma  
 kinase) protein is new. Esp. (I) is cDNA and may encode an  
 alternatively spliced form of the protein. Also new are (1)  
 recombinant DNA vectors comprising a nucleotide sequence encoding an  
 MCK-10 protein or its fusion proteins; (2) engineered host cells  
 contg. the vectors of (1); (3) isolated recombinant MCK-10 receptor  
 protein; (4) fusion proteins comprising MCK-10 linked to a  
 heterologous protein or peptide; (5) oligonucleotides that encode an  
 antisense sequence complementary to (I), able to inhibit translation  
 of the MCK-10 gene; (6) monoclonal antibodies (Ab) binding  
 specifically to an epitope on MCK-10; (7) methods for screening and  
 identifying antagonists of MCK-10 activity; (8) a recombinant vector  
 encoding a truncated MCK-10 with dominant-negative activity, able  
 to inhibit biological activity of MCK-10; (9) engineered cells  
 contg. the vector of (8), and (10) recombinant truncated MCK-10 as  
 described in (8). The specification includes the 3962 bp sequence of  
 (I) encoding MCK-10 and the corresp. derived 919bp protein.  
 USE - Cells expressing MCK-10 (or the protein itself) are used  
 to isolate cpds. that inhibit biological activity of MCK-10. Such  
 cpds. are potentially useful for treatment of proliferative diseases  
 such as cancer. MCK-10 ligands (e.g. Ab) and the new antisense  
 sequences can also be used to modulate (specifically reduce)  
 endogenous activity of the MCK-10 receptor. Ab may also be attached  
 to a cytotoxin or radioisotope for therapeutic use or for in vivo  
 imaging of tumours and metastases. (I) can be used diagnostically to  
 detect abberant gene expression (e.g. in hydridisation tests on  
 biopsy samples). The truncated MCK-10 partic. when expressed from a  
 retroviral vector, can also be used to modulate MCK-10 activity.  
 Dwg.2/6

L7 ANSWER 9 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD  
 AN 94-317002 [39] WPIDS  
 DNC C94-144495  
 TI Extracellular signal regulated kinase (ERK-5) polypeptide  
 - useful for detecting agonists or antagonists for treating e.g.  
 diabetes mellitus, skeletal muscle diseases or Alzheimer's disease..  
 DC B04 D16  
 IN LECHNER, C; MOLLER, N P H; ULLRICH, A  
 PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN  
 CYC 53  
 PI WO 9421781 A2 940929 (9439)\* EN 61 pp  
 RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE  
 W: AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KG KP  
 KR KZ LK LU LV MD MG MN MW NL NO PL PT RO RU SD SE SI SK TJ  
 TT UA UZ VN  
 AU 9465119 A 941011 (9504)  
 US 5459036 A 951017 (9547) 25 pp  
 EP 689588 A1 960103 (9606) EN  
 R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE  
 WO 9421781 A3 941110 (9610)  
 ADT WO 9421781 A2 WO 94-IB89 940318; AU 9465119 A AU 94-65119 940318; US  
 5459036 A US 93-29404 930319; EP 689588 A1 EP 94-912664 940318, WO  
 94-IB89 940318; WO 9421781 A3 WO 94-IB89 940318  
 FDT AU 9465119 A Based on WO 9421781; EP 689588 A1 Based on WO 9421781  
 PRAI US 93-29404 930319  
 AN 94-317002 [39] WPIDS  
 AB WO 9421781 A UPAB: 941122  
 A pure polypeptide (A) comprising a sequence corresp. to the  
 extracellular signal regulated kinase, ERK-5, or a  
 fragment contg. more than 9 contiguous amino acids is new. Also  
 claimed are: (1) an isolated nucleic acid (I) encoding (A); (2) a  
 nucleic acid probe for detecting the presence of ERK-5, comprising  
 (I) or more than 27 contiguous nucleotides of (I); (3) a kit for  
 detecting the presence of ERK-5 RNA in a sample, comprising one or  
 more container means having disposed within the probe of (2); (4) a  
 recombinant nucleic acid molecule comprising 5'-3', a promoter  
 effective to initiate transcription in a host cell and (I); (5) a  
 recombinant nucleic acid molecule comprising a vector and (I); (6) a  
 recombinant nucleic acid molecule comprising a transcriptional  
 region functional in a cell, sequence complementary to an RNA  
 encoding (A), and a transcription termination region functional in  
 the cell; (7) a cell contg. one of the above recombinant nucleic  
 acids; (8) an organism contg. one of the nucleic acids; (9) an  
 antibody (Ab) with binding affinity to (A) or a binding fragment,  
 and no affinity to ERK-1, ERK-2, ERK-3, or ERK-4; (10) a diagnostic  
 kit contg. (i) a 1st container means contg. the Ab or (9); and (ii)  
 a 2nd container means contg. a conjugate comprising a binding  
 partner of the Ab (pref. monoclonal Ab) and a label; and (11) a  
 hybridoma producing the monoclonal Ab (MAb) or (9).  
 (A) comprises all or part of the sequence given in the  
 specification (seq. ID 2) pref. more than 9 contiguous amino  
 acids. (I) comprises all or part of the sequence also given (SEQ ID  
 1) or allelic, mutant or species variations.  
 USE - The polypeptide is useful for detecting agonists or  
 antagonists for use in a pharmaceutical compsn. (claimed) for

treating diabetes mellitus, skeletal muscle diseases, Alzheimer disease or peripheral neuropathies. The probe of (2) is useful for detecting the presence of ERK-5 RNA in samples. Antibodies directed against the polypeptide are useful for detecting (A) in samples and for measuring the amt. of (A) in samples, by measuring immunocomplexes formed.

Dwg.0/6

ABEQ US 5459036 A UPAB: 951128

Isolated nucleic acid molecule encodes a polypeptide having an amino acid sequence of at least 9 contiguous amino acids having the sequence given in the specification. Polypeptide has the full length ERK-5 amino acid sequence also given in the specification. Also claimed are a nucleic acid probe comprising the isolated nucleic acid molecule, a kit for detecting the presence of ERK-5 RNA; and a transformant cell contg. the nucleic acid.

USE - Detecting the presence of ERK-5 RNA in a sample. Acting as agonist or antagonist for ERK-5 associated activity, e.g. for treating diabetes mellitus skeletal muscle disorders, Alzheimer's disease and peripheral neuropathies. Dosage is 0.001-50 (0.1-1.0) mg/kg given once or more per day. Admin. is parenteral by injection or infusion e.g. intravenous, intraperitoneal, intramuscular or subcutaneous.

Dwg.0/8

L7 ANSWER 10 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD

AN 94-183501 [22] WPIDS

DNN N94-144837 DNC C94-083203

TI DNA encoding Flk-1, a tyrosine kinase receptor for vascular endothelial growth factor - used to express recombinant Flk-1 for screening for ligands useful for modulating vasculogenesis and angiogenesis e.g. for treating cancer.

DC B04 D16 S03

IN MILLAUER, B; RISAU, W; ULLRICH, A

PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN; (PLAC) MAX PLANCK SCI PROMOTION INST

CYC 40

PI WO 9411499 A1 940526 (9422)\* 99 pp

RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE

W: AU BG BR BY CA CZ FI HU JP KP KR KZ LV NO NZ PL RO RU SK UA  
UZ

AU 9455627 A 940608 (9435)

EP 669978 A1 950906 (9540) EN

R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

CN 1094445 A 941102 (9543)

ADT WO 9411499 A1 WO 93-EP3191 931115; AU 9455627 A AU 94-55627 931115; EP 669978 A1 WO 93-EP3191 931115, EP 94-900810 931115; CN 1094445 A CN 93-115345 931113

FDT AU 9455627 A Based on WO 9411499; EP 669978 A1 Based on WO 9411499

PRAI US 92-975750 921113; US 93-38596 930326

AN 94-183501 [22] WPIDS

AB WO 9411499 A UPAB: 940722

A recombinant DNA vector (1) contg. a nucleotide sequence encoding Flk-1, a receptor for vascular endothelial growth factor (VEGF), is new. The Flk-1 gene is operatively associated with a regulatory sequence that controls gene expression in a host.

\*< Arti Shah- Stic Searcher- 308-4259 >\*

Also claimed are: (1) a vector (II) as above but encoding an Flk-1 fusion protein; (2) an engineered host cell or cell lines contg. (I) or (II); (3) an isolated Flk-1 receptor protein; (4) a fusion protein comprising Flk-1 linked to a heterologous protein or peptide sequence; (5) an oligonucleotide encoding an antisense sequence complementary to a portion of the Flk-1 sequence, which inhibits translation of the Flk-1 gene in a cell; (6) a monoclonal antibody (MAb) which is immunospecific for an epitope of Flk-1; (7) a VEGF agonist which is a MAb specific for an epitope of Flk-1; (8) a recombinant vector (III) contg. a nucleotide sequence encoding a truncated Flk-q which has dominant negative activity which inhibits the cellular effects of VEGF binding; (9) an engineered cell line contg. (III) which expresses truncated Flk-1; (10) an engineered cell line contg. (III) which produces infectious retrovirus particles expressing truncated Flk-1; (11) an isolated recombinant truncated Flk-1 which has dominant negative activity and which inhibits the cellular effects of VEGF binding.

USE - Flk-1 tyrosine kinase receptor expression has been found to be associated with endothelial cells and VEGF has been identified as a high affinity ligand of the receptor. The results indicate a major role for Flk-1 in the signalling system involved in vasculogenesis and angiogenesis. Pharmaceutical reagents designed to inhibit the Flk-1/VEGF interaction may be useful in inhibiting tumour growth. VEGF and/or VEGF agonists may be used to promote wound healing. The sol. Flk-1 receptor produced using the expression systems described may be used to screen peptide libraries for molecules which inhibit the Flk-1/VEGF binding. The engineered cell lines of the invention, which express the receptor on their surface may be used to screen and identify VEGF agonists and antagonists. A transdominant negative form of the Flk-1 molecule has also been identified, which can be used to treat diseases resulting from abnormal proliferation of blood vessels, such as rheumatoid arthritis, retinopathies and growth of solid tumours.

Dwg.1/14

L7 ANSWER 11 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD  
 AN 93-086338 [11] WPIDS  
 DNC C93-038066  
 TI Use of mutated growth factor e.g. EGF receptors - for treatment of  
 mammary, ovarian or lung carcinoma.  
 DC B04 D16  
 IN REDEMANN, N; ULLRICH, A; REDEMANN, N H; ULRICH, A;  
 REDEMAN, N H  
 PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN  
 CYC 40  
 PI DE 4129533 A1 930311 (9311)\* 10 pp  
 WO 9305148 A1 930318 (9312) DE 43 pp  
 RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA SE  
 W: AT AU BB BG BR CA CH CS DE DK ES FI GB HU JP KP KR LK LU MG  
 MN MW NL NO PL RO RU SD SE  
 AU 9225185 A 930405 (9330)  
 CN 1071586 A 930505 (9409)  
 PT 100844 A 940531 (9421)  
 FI 9401053 A 940408 (9424)  
 NO 9400778 A 940504 (9427)

\*< Arti Shah- Stic Searcher- 308-4259 >\*

JP 07502884 W 950330 (9521)  
 NZ 244239 A 950726 (9535)  
 EP 667899 A1 950823 (9538) DE

R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE

ADT DE 4129533 A1 DE 91-4129533 910905; WO 9305148 A1 WO 92-EP2058  
 920907; AU 9225185 A AU 92-25185 920907; CN 1071586 A CN 92-111396  
 920905; PT 100844 A PT 92-100844 920904; FI 9401053 A WO 92-EP2058  
 920907, FI 94-1053 940304; NO 9400778 A WO 92-EP2058 920907, NO  
 94-778 940304; JP 07502884 W WO 92-EP2058 920907, JP 93-504969  
 920907; NZ 244239 A NZ 92-244239 920907; EP 667899 A1 EP 92-918949  
 920907, WO 92-EP2058 920907  
 FDT AU 9225185 A Based on WO 9305148; JP 07502884 W Based on WO 9305148;  
 EP 667899 A1 Based on WO 9305148

PRAI DE 91-4129533 910905

AN 93-086338 [11] WPIDS

AB DE 4129533 A UPAB: 931122

Claimed is a mutated growth factor receptor (R) as a medicament. The R pref. comprises (i) tyrosine kinase activity loss of the wild type receptor, (ii) a deletion in the domain of the tyrosine kinase, (iii) a deletion in the cytoplasmic domain of the tyrosine kinase, (iv) a mutated receptor tyrosine kinase i.e. mutated epidermal growth factor receptor (E-R), (v) a point mutation at position 721 of E-R, pref. having alanine, (vi) E-R having a deletion of 533-C-terminal amino acids, or (vii) a point mutation of the wild type receptor.

Also claimed is a medicament having the receptors in liposomes or DNA fragments in recombinant retroviral viruses such as pNTK-HER-K721A and/or pNTK-HERCD-533 (DSM 6678 and DSM6679).

USE/ADVANTAGE - The medicament and the mutated receptor are used for the treatment of cancer, caused by over-production of Rs, such as breast, ovary and/or lung cancers (claimed). In contrast to prior art cancer treatments which involve interference with the DNA metabolism, the mutated receptors inhibit the transformation of an extra cellular growth signal so that it does not result in an intracellular growth signal. This effect was observed with co-expression of wild-type receptors

Dwg.0/3

L7 ANSWER 12 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD

AN 89-233846 [32] WPIDS

DNN N89-178288 DNC C89-104136

TI Treatment of tumour cells - by inhibiting growth factor receptor function with monoclonal antibody specifically HER2 receptor.

DC B04 D16 S03

IN HUDZIAK, R M; SHEPARD, H; ULLRICH, A

PA (GETH) GENENTECH INC

CYC 1

PI WO 8906692 A 890727 (8932)\* EN 51 pp

W: JP

JP 03502885 W 910704 (9133)

ADT WO 8906692 A WO 89-US51 890105; JP 03502885 W JP 89-501807 890105

PRAI US 88-143912 880112; US 88-147461 880125

AN 89-233846 [32] WPIDS

AB WO 8906692 A UPAB: 930923

A monoclonal antibody (mAb1) specifically binding the extracellular

domain of the HER2 receptor is claimed. The antibody is capable of inhibiting the HER2 receptor function and of inhibiting serum activation of HER2 receptor function.

Also claimed is an assay for detecting a tumour comprising exposing cells to mAb1 and determining the extent of binding of the antibodies to the cells. Method of treating tumour cells comprises (1) administering an amt. of antibodies capable of inhibiting growth factor receptor function, and (2) administering a cytotoxic factor (I).

Also claimed is an assay for receptors and other proteins with increased tyrosine kinase activity comprising (a) exposing cells suspected to be TNF-x sensitive to TNF-x; (b) isolating those cells which are TNF-x resistant; (c) screening the isolated cells for increased tyrosine kinase, and (d) isolating receptors and other proteins having increased tyrosine kinase activity.

USE - MAb1 is useful for in vivo tumour therapy. Dosage is 0.1-10mg/kg. The antibodies may be used for therapy of malignant or benign tumours where the abnormal growth rate of the tumour is dependent on growth factor receptors.

0/8

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FILE LAST UPDATED: 20 Jun 1996 (960620/ED)

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L14 2 SEA FILE=CAPLUS CIOSEK T?/AU  
L15 353 SEA FILE=CAPLUS ULLRICH A?/AU  
L16 9 SEA FILE=CAPLUS MILLAUER B?/AU  
L18 3 SEA FILE=CAPLUS MDK1/BI  
L20 2 SEA FILE=CAPLUS (L14 OR L15 OR L16) AND L18

=> d bib ab 120 1-2

L20 ANSWER 1 OF 2 CAPLUS COPYRIGHT 1996 ACS  
AN 1995:972773 CAPLUS  
DN 124:82771  
TI Cloning, characterization, and differential expression of mouse developmental kinase MDK2 and MDK5, two novel receptor tyrosine kinases of the eck/eph family  
AU Clossek, Thomas; Lerch, Markus M.; Ullrich, Axel  
CS Department of Molecular Biology, Max-Planck-Institut fuer Biochimie, Martinsried, 82152, Germany  
SO Oncogene (1995), 11(10), 2085-95  
CODEN: ONCNES; ISSN: 0950-9232  
DT Journal  
LA English  
AB Using a polymerase chain reaction-based strategy for the cloning of developmentally regulated receptor tyrosine kinases, we identified two novel members of the eck/eph-related subfamily which, in analogy with the recently identified mouse developmental kinase 1 (MDK1), were designated MDK2 and MDK5. MDK2 is highly homologous to the mouse kinase Myk-1 and the human kinase Htk, whereas MDK5 represents the mouse homolog of human Hek2. Northern blot analyses of adult mouse tissues revealed a 4.7 kb transcript of MDK2 and a 4.8 kb transcript of MDK5 in various organ systems, including lung, liver, kidney, intestine, muscle heart, and, in the case of MDK5, also the brain. In addn. to the full-length transcripts, smaller fragments were identified that probably



represent truncated receptors. Northern blot anal. and in situ hybridization of mouse embryos indicated abundant expression during embryonic development, with preferential involvement of tissues of epithelial and endothelial origin for both kinases and of the spinal cord gray matter for MDK5. Unlike most other members of the eck/eph-related subfamily, the expression of MDK2 and MDK5 is not primarily restricted to neuronal structures, and their abundant presence in various organ systems during embryonic development suggests an important role in gestational growth and differentiation.

L20 ANSWER 2 OF 2 CAPLUS COPYRIGHT 1996 ACS  
AN 1995:307905 CAPLUS  
DN 122:183817  
TI Identification of alternatively spliced mRNAs encoding variants of  
MDK1, a novel receptor tyrosine kinase expressed in the  
murine nervous system  
AU Ciossek, Thomas; Millauer, Birgit; Ullrich,  
Axel  
CS Department of Molecular Biology, Max-Planck-Institut fuer Biochemie,  
Martinsried, 82152, Germany  
SO Oncogene (1995), 10(1), 97-108  
CODEN: ONCNES; ISSN: 0950-9232  
DT Journal  
LA English  
AB A novel member of the eck/eph family of receptor tyrosine kinases  
(RTKs), termed mouse developmental kinase 1 (MDK1), was  
identified and shown to be closely related to the Eek, Ehk1/Cek7,  
Ehk2, Cek4/Mek4/hek, and Sek/Cek8 subfamily. Northern blot anal.  
revealed MDK1 mRNA transcripts of 6.8, 5.7, 4.0, 3.2, and  
2.6 kb that encode apparent splice variants. Sequence analyses of  
MDK1 cDNA clones from adult mouse brain predict the  
existence of .gtoreq.5 isoforms, including 2 truncated receptor  
variants lacking the kinase domain. Northern blot and in situ  
hybridization anal. indicate that in the adult mouse MDK1  
RNA expression is restricted to brain, testes, and spleen. The  
distinct patterns of MDK1 gene expression during mouse  
development suggest an important role in the formation of neuronal  
structures and possibly other morphogenic processes.

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S2	999	AU=((ULLRICH, A?) OR (ULLRICH A?))
S3	29	AU=((MILLAUER, B?) OR (MILLAUER B?))
S4	10	MDK1 OR (MDK(W)1)
S5	80999	SIGNAL(W)TRANSDUC?
S6	36103	TYROSINE(W)KINASE? ?
S7	6	(S1 OR S2 OR S3) AND S4

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S11 2 RD S7 (unique items)

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11/7/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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09553237 96074837

Cloning, characterization, and differential expression of MDK2 and MDK5, two novel receptor tyrosine kinases of the eck/eph family.

\*\*\*\*Ciossek T\*\*\*\*; Lerch MM; \*\*\*\*Ullrich A\*\*\*\*

Department of Molecular Biology, Max-Planck-Institut fur Biochemie, Martinsried, Germany.

Oncogene (ENGLAND) Nov 16 1995, 11 (10) p2085-95, ISSN 0950-9232

Journal Code: ONC

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Using a polymerase chain reaction-based strategy for the cloning of developmentally regulated receptor tyrosine kinases, we identified two novel members of the eck/eph-related subfamily which, in analogy with the recently identified mouse developmental kinase 1 (\*\*\*\*MDK1\*\*\*\*), were designated MDK2 and MDK5. MDK2 is highly homologous to the mouse kinase Myk-1 and the human kinase Htk, whereas MDK5 represents the mouse homologue of human Hek2. Northern blot analyses of adult mouse tissues revealed a 4.7 kb transcript of MDK2 and a 4.8 kb transcript of MDK5 in various organ systems, including lung, liver, kidney, intestine, muscle, heart, and, in the case of MDK5, also the brain. In addition to the full-length transcripts, smaller fragments were identified that probably represent truncated receptors. Northern blot analysis and in situ hybridization of mouse embryos indicated abundant expression during embryonic development, with preferential involvement of tissues of epithelial and endothelial origin for both kinases and of the spinal cord gray matter for MDK5. Unlike most other members of the eck/eph-related subfamily, the expression of MDK2 and MDK5 is not primarily restricted to neuronal structures, and their abundant presence in various organ systems during embryonic development suggests an important role in gestational growth and differentiation.

11/7/2 (Item 2 from file: 155)  
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09194729 95124729

Identification of alternatively spliced mRNAs encoding variants of  
\*\*\*\*MDK1\*\*\*\*, a novel receptor tyrosine kinase expressed in the murine  
nervous system.

\*\*\*\*Ciossek T\*\*\*\*; \*\*\*\*Millauer B\*\*\*\*; \*\*\*\*Ullrich A\*\*\*\*  
Department of Molecular Biology, Max-Planck-Institut Fur Biochemie,  
Martinsried, Germany.

Oncogene (ENGLAND) Jan 5 1995, 10 (1) p97-108, ISSN 0950-9232  
Journal Code: ONC

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A novel member of the eck/eph family of receptor tyrosine kinases (RTKs),  
termed mouse developmental kinase 1 (\*\*\*\*MDK1\*\*\*\*), was identified and  
shown to be closely related to the Eek, Ehk1/Cek7, Ehk2, Cek4/Mek4/hek and  
Sek/Cek8 subfamily. Northern blot analysis revealed \*\*\*\*MDK1\*\*\*\* mRNA  
transcripts of 6.8, 5.7, 4.0, 3.2 and 2.6 kb that encode apparent splice  
variants. Sequence analyses of \*\*\*\*MDK1\*\*\*\* cDNA clones from adult mouse  
brain predict the existence of at least five isoforms, including two  
truncated receptor variants lacking the kinase domain. Northern blot and in  
situ hybridization analysis indicate that in the adult mouse \*\*\*\*MDK1\*\*\*\*  
RNA expression is restricted to brain, testes and spleen. The distinct  
patterns of \*\*\*\*MDK1\*\*\*\* gene expression during mouse development suggest  
an important role in the formation of neuronal structures and possibly  
other morphogenic processes.

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